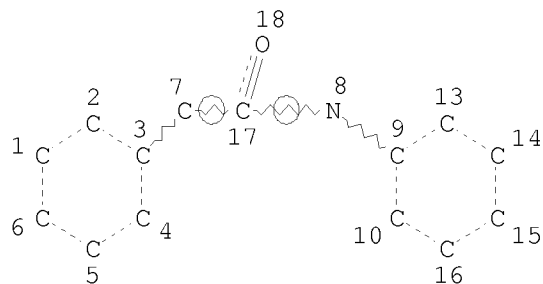


=> d 11
L1 HAS NO ANSWERS
L1 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

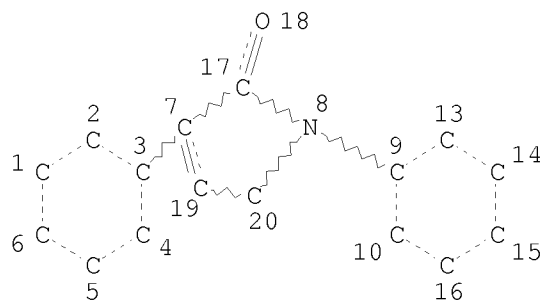
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

=> d his 13

(FILE 'REGISTRY' ENTERED AT 09:27:52 ON 26 FEB 2008)
L3 8571 S L1 FUL

=> d 116
L16 HAS NO ANSWERS
L16 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

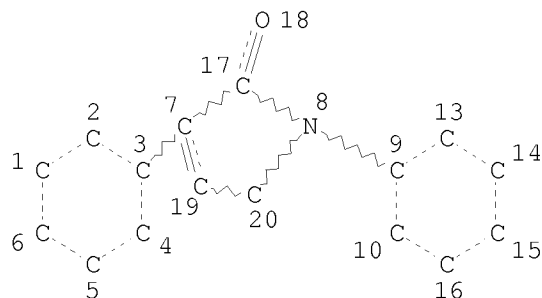
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

=> d his 117

(FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)
L17 984 SEARCH L16 SSS SUB=L3 FUL

=> d 118
L18 HAS NO ANSWERS
L18 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 7
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

=> d his 119

(FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)
L19 908 SEARCH L18 SSS SUB=L3 FUL

=> d his 120-128

(FILE 'REGISTRY' ENTERED AT 09:48:05 ON 26 FEB 2008)
L20 328 S L19 AND (PYRROL?(L)DIONE)
L21 580 S L19 NOT L20
L22 125 S L21 AND (DIOXO? OR DIKETO?)
L23 455 S L21 NOT L22

FILE 'CAPLUS' ENTERED AT 09:55:59 ON 26 FEB 2008
L24 62 S L23
L25 4 S L24 AND (DEPRES? OR ANXI? OR CNS)
L26 58 S L24 NOT L25
L27 50 S L26 AND PY<=2002
L28 21 S L27 AND P/DT

=> d bib abs 125 1-4

L25 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:625334 CAPLUS
DN 145:271603
TI Diaryl substituted pyrrolidinones and pyrrolones as 5-HT2C inhibitors:
Synthesis and biological evaluation
AU Micheli, Fabrizio; Pasquarello, Alessandra; Tedesco, Giovanna; Hamprecht,
Dieter; Bonanomi, Giorgio; Checchia, Anna; Jaxa-Chamiec, Albert; Damiani,
Federica; Davalli, Silvia; Donati, Daniele; Gallotti, Chiara; Petrone,
Marcella; Rinaldi, Marilisa; Riley, Graham; Terreni, Silvia; Wood, Martyn

CS GlaxoSmithKline Psychiatry Centre of Excellence for Drug Discovery,
Verona, 4, 37135, Italy
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(15), 3906-3912
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
AB Within the continuous quest for the discovery of novel compds. able to
treat anxiety and depression, the generation of a
pharmacophore model for 5-HT_{2C} receptor antagonists and the discovery of a
new class of potent and selective 5-HT_{2C} mols. are reported.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:1019875 CAPLUS
DN 141:406136
TI Compositions of a cyclooxygenase-2 selective inhibitor and a peroxisome
proliferator activated receptor agonist for the treatment of
ischemia-mediated central nervous system disorders
IN Needleman, Philip; Obukowicz, Mark G.; Arneric, Stephen P.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004100895	A2	20041125	WO 2004-US14741	20040512
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2005107387 A1 20050519 US 2004-844269 20040512				
PRAI US 2003-470240P	P	20030513		

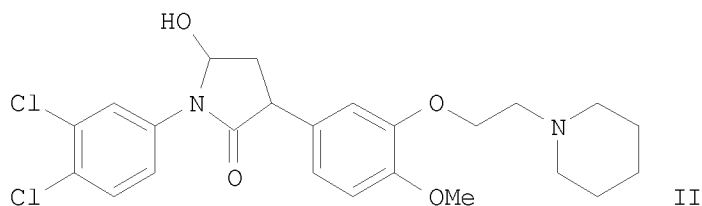
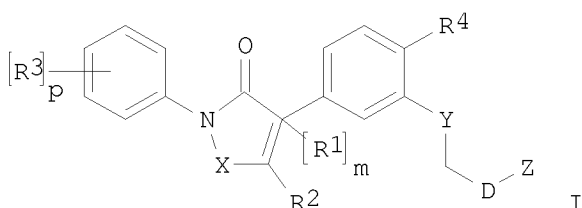
OS MARPAT 141:406136
AB The invention provides compns. and methods for the treatment of
ischemia-mediated central nervous system disorders. More particularly,
the invention provides a combination therapy for the treatment of a
central nervous system ischemia-mediated disorder comprising the
administration to a subject of a peroxisome proliferator activated
receptor agonist in combination with a cyclooxygenase-2 selective
inhibitor.

L25 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:756686 CAPLUS
DN 141:277494
TI Preparation of diaryl substituted pyrrolidinones and pyrrolones having
activity at 5-HT_{2C} receptor
IN Damiani, Federica; Hamprecht, Dieter; Micheli, Fabrizio; Pasquarello,
Alessandra; Tedesco, Giovanna
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004078718	A1	20040916	WO 2004-EP1843	20040224
	WO 2004078718	A8	20050526		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI			
	RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	EP 1599445	A1	20051130	EP 2004-713874	20040224
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
	JP 2006519241	T	20060824	JP 2006-504465	20040224
	US 2006205788	A1	20060914	US 2006-548118	20060518
PRAI	GB 2003-5024	A	20030305		
	WO 2004-EP1843	W	20040224		
OS	MARPAT 141:277494				
GI					



AB The title compds. [I; R1 = H, F, Cl, OH, alkyl, cycloalkyl, cycloalkyloxy, alkoxy or haloalkoxy; m = 0-1; R2 = H, halo, CN, NO2, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or dialkylamino or an N-linked 4-7 membered heterocyclic group; X = CH2CH2, CH:CH, (CH2)3, C(CH3)2, CH:CHCH2, CH2CH:CH or CHR5 (wherein R5 = H, halo, OH, CN, NO2, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy or alkylthio); R3 = halo, CN, alkyl, cycloalkyl, cycloalkyloxy, alkoxy, alkylthio, OH, NH2, mono- or dialkylamino, etc.; p = 0-3; R4 = H, halo, OH, CN, NO2, alkyl, alkanoyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or dialkylamino or an N-linked 4-7 membered heterocyclic group; Y = O, S, CH2 or NR10 (wherein R10 = H, alkyl); D = a single bond, CH2, (CH2)2 or CH:CH; Z = NR11R12 (where R11 and R12 = H, alkyl, (un)substituted N-linked or C-linked 4-7 membered

heterocyclic group)] and their pharmaceutically acceptable salts, useful in treating, for example, depression and anxiety, were prepared E.g., a multi-step synthesis of II, was given. All exemplified compds. I were tested for their affinity for the 5-HT_{2c} receptor, and were found to have pK_i values >5.8. The pharmaceutical composition comprising the compound I is disclosed.

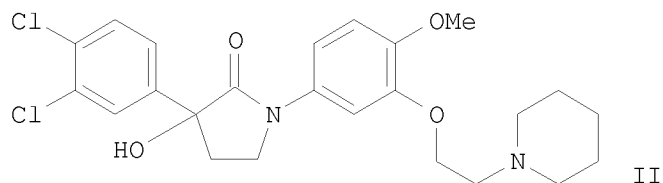
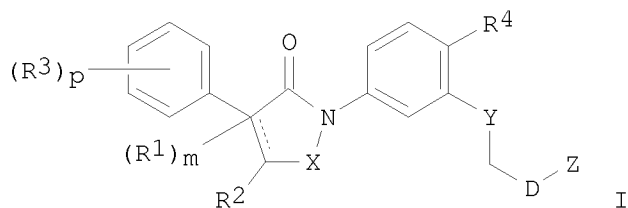
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:855908 CAPLUS
DN 139:350638
TI 3-Aryl-1-[4-alkoxy-3-[2-(piperidin-1-yl)ethoxy]phenyl]pyrrolidin-2-ones and analogs with affinity at 5-HT_{2C} receptors, and use thereof in therapy, particularly as antidepressants and anxiolytics, and their preparation and pharmaceutical compositions
IN Damiani, Federica; Hamprecht, Dieter; Jaxa-Chamiec, Albert Andrzej; Micheli, Fabrizio; Pasquarello, Alessandra; Tedesco, Giovanna
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003089409	A1	20031030	WO 2003-EP4180	20030417
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003222832	A1	20031103	AU 2003-222832	20030417
	EP 1497265	A1	20050119	EP 2003-718783	20030417
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2005529117	T	20050929	JP 2003-586130	20030417
	US 2005203079	A1	20050915	US 2005-511769	20050502
PRAI	GB 2002-9029	A	20020419		
	GB 2002-20781	A	20020906		
	WO 2003-EP4180	W	20030417		
OS	MARPAT 139:350638				
GI					



AB Title compds. I and their pharmaceutically acceptable salts are disclosed [wherein: R1 = H, OH, F, Cl, alkyl, cycloalkyl, cycloalkyloxy, alkoxy or haloalkoxy; m = 0 or 1; R2 = H, halo, cyano, NO2, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or di-C1-6alkylamino, or N-linked 4-7 membered heterocyclic; X = CH2CH2, CH:CH, (CH2)3, C(CH3)2, CH:CHCH2, CH2CH:CH, or CHR5; R3 = halo, cyano, alkyl, cycloalkyl, cycloalkyloxy, C1-6alkoxy, C1-6alkylthio, OH, amino, mono- or di-C1-6alkylamino, N-linked 4-7 membered heterocyclic, NO2, haloalkyl, haloalkoxy, aryl, arylalkyl, arylalkyloxy, arylalkylthio, COOR6, CONR7R8, or COR9; R4 = H, halo, OH, cyano, NO2, alkyl, alkanoyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy, alkylthio, amino, mono- or di-alkylamino or N-linked 4-7 membered heterocyclic; R5 = H, halo, OH, cyano, NO2, alkyl, cycloalkyl, cycloalkyloxy, haloalkyl, alkoxy, haloalkoxy or alkylthio; R6, R7, R8, and R9 = H or alkyl; p = 0, 1, 2, or 3; Y = O, S, CH2, or NR10; R10 = H or alkyl; D = bond, CH2, (CH2)2, or CH:CH; Z = (un)substituted C-linked 4-7 membered heterocyclic group containing at least 1 N, (un)substituted N-linked 4-7 membered heterocyclic, or Z = NR11R12; R11 and R12 = H or alkyl]. Methods of preparation and uses of I in therapy, particularly for treating CNS disorders such as depression and anxiety, are also disclosed. The affinities of compds. I for 5-HT2C receptors were determined by assessing their ability to displace [3H]-mesulergine from rat or human 5-HT2C clones expressed in 293 cells in vitro, as described in WO 94/04533. All example compds. were so tested and had pKi values >5.8. Some compds. I show a considerably higher affinity, in the range of 7.0 to >9.0 in human cells. Approx. 45 synthetic examples and approx. 75 precursor preps. are given. For instance, 3,4-dichlorophenylacetic acid underwent a sequence of (1) α -lithiation and allylation, (2) amidation with 2-(5-amino-2-methoxyphenoxy)ethyl acetate, (3) OsO4-catalyzed glycolation of the alkene, and periodate oxidation of the glycol with cyclic hemiaminal formation, to give a 5-hydroxy-2-pyrrolidinone derivative, (4) reduction of the latter to remove 5-hydroxy, (5) saponification of the acetate ester sidechain to an alc., (6) conversion of the alc. to a mesylate ester, and (7) aminolysis of the mesylate with piperidine in the presence of K2CO3 and NaI, followed by benzylic hydroxylation with air over 18 h, to give title compound II.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT